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☐ 1: [P29473](#). Reports Nitric-oxide synt...[gi:266647]

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**LOCUS** P29473 1205 aa linear MAM 20-FEB-2007  
**DEFINITION** Nitric-oxide synthase, endothelial (EC-NOS) (NOS type III) (NOSIII) (Endothelial NOS) (eNOS) (Constitutive NOS) (cNOS).  
**ACCESSION** P29473  
**VERSION** P29473 GI:266647  
**DBSOURCE** swissprot: locus NOS3\_BOVIN, accession [P29473](#);  
 class: standard.  
 created: Apr 1, 1993.  
 sequence updated: Jan 23, 2007.  
 annotation updated: Feb 20, 2007.  
 xrefs: [M99057.1](#), [AAA30667.1](#), [M89952.1](#), [AAA30494.1](#), [M95674.1](#),  
[AAA30669.1](#), [A38943](#), [1D0CA](#), [1D0CB](#), [1D0OA](#), [1D0OB](#), [1D1VA](#), [1D1VB](#),  
[1D1WA](#), [1D1WB](#), [1D1XA](#), [1D1XB](#), [1D1YA](#), [1D1YB](#), [1DM6A](#), [1DM6B](#), [1DM7A](#),  
[1DM7B](#), [1DM8A](#), [1DM8B](#), [1DMIA](#), [1DMIB](#), [1DMJA](#), [1DMJB](#), [1DMKA](#), [1DMKB](#),  
[1ED4A](#), [1ED4B](#), [1ED5A](#), [1ED5B](#), [1ED6A](#), [1ED6B](#), [1FOIA](#), [1FOIB](#), [1FOJA](#),  
[1FOJB](#), [1FOLA](#), [1FOLB](#), [1FOOA](#), [1FOOB](#), [1FOPA](#), [1FOPB](#), [1I83A](#), [1I83B](#),  
[1NSEA](#), [1NSEB](#), [1P6LA](#), [1P6LB](#), [1P6MA](#), [1P6MB](#), [1P6NA](#), [1P6NB](#), [1Q2OA](#),  
[1Q2OB](#), [1RS8A](#), [1RS8B](#), [1RS9A](#), [1RS9B](#), [1ZZSA](#), [1ZZSB](#), [1ZZTA](#), [1ZZTB](#),  
[2NSEA](#), [2NSEB](#), [3NSEA](#), [3NSEB](#), [4NSEA](#), [4NSEB](#), [5NSEA](#), [5NSEB](#), [6NSEA](#),  
[6NSEB](#), [7NSEA](#), [7NSEB](#), [8NSEA](#), [8NSEB](#), [9NSEA](#), [9NSEB](#)  
 xrefs (non-sequence databases): UniGene:Bt.4662, KEGG:bta:287024,  
 LinkHub:P29473, InterPro:IPR003097, InterPro:IPR001094,  
 InterPro:IPR008254, InterPro:IPR001709, InterPro:IPR004030,  
 InterPro:IPR012144, InterPro:IPR001433, Pfam:PF00667, Pfam:PF00258,  
 Pfam:PF00175, Pfam:PF02898, PIRSF:PIRSF000333, PRINTS:PR00369,  
 PRINTS:PR00371, PROSITE:PS50902, PROSITE:PS60001  
**KEYWORDS** 3D-structure; Blood coagulation; Calcium; Calmodulin-binding; FAD;  
 FMN; Heme; Iron; Lipoprotein; Metal-binding; Myristate; NADP;  
 Oxidoreductase; Palmitate; Phosphorylation; Zinc.  
**SOURCE** Bos taurus (cattle)  
**ORGANISM** *Bos taurus*  
 Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;  
 Mammalia; Eutheria; Laurasiatheria; Cetartiodactyla; Ruminantia;  
 Pecora; Bovidae; Bovinae; Bos.  
**REFERENCE** 1 (residues 1 to 1205)  
**AUTHORS** Lamas,S., Marsden,P.A., Li,G.K., Tempst,P. and Michel,T.  
**TITLE** Endothelial nitric oxide synthase: molecular cloning and  
 characterization of a distinct constitutive enzyme isoform  
**JOURNAL** Proc. Natl. Acad. Sci. U.S.A. 89 (14), 6348-6352 (1992)  
**PUBMED** [1378626](#)  
**REMARK** NUCLEOTIDE SEQUENCE [MRNA].  
**REFERENCE** 2 (residues 1 to 1205)

AUTHORS Nishida,K., Harrison,D.G., Navas,J.P., Fisher,A.A., Dockery,S.P., Uematsu,M., Nerem,R.M., Alexander,R.W. and Murphy,T.J.

TITLE Molecular cloning and characterization of the constitutive bovine aortic endothelial cell nitric oxide synthase

JOURNAL J. Clin. Invest. 90 (5), 2092-2096 (1992)

PUBMED [1385480](#)

REMARK NUCLEOTIDE SEQUENCE [MRNA].

REFERENCE 3 (residues 1 to 1205)

AUTHORS Sessa,W.C., Harrison,J.K., Barber,C.M., Zeng,D., Durieux,M.E., D'Angelo,D.D., Lynch,K.R. and Peach,M.J.

TITLE Molecular cloning and expression of a cDNA encoding endothelial cell nitric oxide synthase

JOURNAL J. Biol. Chem. 267 (22), 15274-15276 (1992)

PUBMED [1379225](#)

REMARK NUCLEOTIDE SEQUENCE [MRNA].

TISSUE=Aortic endothelium

REFERENCE 4 (residues 1 to 1205)

AUTHORS Busconi,L. and Michel,T.

TITLE Endothelial nitric oxide synthase. N-terminal myristoylation determines subcellular localization

JOURNAL J. Biol. Chem. 268 (12), 8410-8413 (1993)

PUBMED [7682550](#)

REMARK MYRISTOYLATION AT GLY-2.

REFERENCE 5 (residues 1 to 1205)

AUTHORS Robinson,L.J. and Michel,T.

TITLE Mutagenesis of palmitoylation sites in endothelial nitric oxide synthase identifies a novel motif for dual acylation and subcellular targeting

JOURNAL Proc. Natl. Acad. Sci. U.S.A. 92 (25), 11776-11780 (1995)

PUBMED [8524847](#)

REMARK PALMITOYLATION AT CYS-15 AND CYS-26.

REFERENCE 6 (residues 1 to 1205)

AUTHORS Boo,Y.C., Hwang,J., Sykes,M., Michell,B.J., Kemp,B.E., Lum,H. and Jo,H.

TITLE Shear stress stimulates phosphorylation of eNOS at Ser(635) by a protein kinase A-dependent mechanism

JOURNAL Am. J. Physiol. 283, H1819-H1828 (2002)

PUBMED [12384459](#)

REMARK PHOSPHORYLATION AT THR-497; SER-635 AND SER-1179.

REFERENCE 7 (residues 1 to 1205)

AUTHORS Raman,C.S., Li,H., Martasek,P., Kral,V., Masters,B.S. and Poulos,T.L.

TITLE Crystal structure of constitutive endothelial nitric oxide synthase: a paradigm for pterin function involving a novel metal center

JOURNAL Cell 95 (7), 939-950 (1998)

PUBMED [9875848](#)

REMARK X-RAY CRYSTALLOGRAPHY (1.9 ANGSTROMS) OF 67-482.

REFERENCE 8 (residues 1 to 1205)

AUTHORS Li,H., Raman,C.S., Martasek,P., Kral,V., Masters,B.S. and Poulos,T.L.

TITLE Mapping the active site polarity in structures of endothelial nitric oxide synthase heme domain complexed with isothioureas

JOURNAL J. Inorg. Biochem. 81 (3), 133-139 (2000)

PUBMED [11051558](#)

REMARK X-RAY CRYSTALLOGRAPHY (1.86 ANGSTROMS) OF 67-482.

REFERENCE 9 (residues 1 to 1205)

AUTHORS Li,H., Raman,C.S., Martasek,P., Masters,B.S. and Poulos,T.L.

TITLE Crystallographic studies on endothelial nitric oxide synthase complexed with nitric oxide and mechanism-based inhibitors

JOURNAL Biochemistry 40 (18), 5399-5406 (2001)  
 PUBMED [11331003](#)  
 REMARK X-RAY CRYSTALLOGRAPHY (1.93 ANGSTROMS).  
 REFERENCE 10 (residues 1 to 1205)  
 AUTHORS Raman,C.S., Li,H., Martasek,P., Southan,G., Masters,B.S. and Poulos,T.L.  
 TITLE Crystal structure of nitric oxide synthase bound to nitro indazole reveals a novel inactivation mechanism  
 JOURNAL Biochemistry 40 (45), 13448-13455 (2001)  
 PUBMED [11695891](#)  
 REMARK X-RAY CRYSTALLOGRAPHY (1.65 ANGSTROMS).  
 REFERENCE 11 (residues 1 to 1205)  
 AUTHORS Raman,C.S., Li,H., Martasek,P., Babu,B.R., Griffith,O.W., Masters,B.S. and Poulos,T.L.  
 TITLE Implications for isoform-selective inhibitor design derived from the binding mode of bulky isothioureas to the heme domain of endothelial nitric-oxide synthase  
 JOURNAL J. Biol. Chem. 276 (28), 26486-26491 (2001)  
 PUBMED [11331290](#)  
 REMARK X-RAY CRYSTALLOGRAPHY (1.93 ANGSTROMS).  
 REFERENCE 12 (residues 1 to 1205)  
 AUTHORS Kotsonis,P., Frohlich,L.G., Raman,C.S., Li,H., Berg,M., Gerwig,R., Groehn,V., Kang,Y., Al-Masoudi,N., Taghavi-Moghadam,S., Mohr,D., Munch,U., Schnabel,J., Martasek,P., Masters,B.S., Strobel,H., Poulos,T., Matter,H., Pfeleiderer,W. and Schmidt,H.H.  
 TITLE Structural basis for pterin antagonism in nitric-oxide synthase. Development of novel 4-oxo-pteridine antagonists of (6R)-5,6,7,8-tetrahydrobiopterin  
 JOURNAL J. Biol. Chem. 276 (52), 49133-49141 (2001)  
 PUBMED [11590164](#)  
 REMARK X-RAY CRYSTALLOGRAPHY (2.35 ANGSTROMS).  
 COMMENT On Mar 15, 2005 this sequence version replaced [gi:1083055](#).  
 [FUNCTION] Produces nitric oxide (NO) which is implicated in vascular smooth muscle relaxation through a cGMP-mediated signal transduction pathway. No mediates vascular endothelial growth factor (VEGF)-induced angiogenesis in coronary vessels and promotes blood clotting through the activation of platelets.  
 [CATALYTIC ACTIVITY] L-arginine + n NADPH + m O(2) = citrulline + nitric oxide + n NADP(+).  
 [COFACTOR] Heme group.  
 [COFACTOR] Binds 1 FAD.  
 [COFACTOR] Binds 1 FMN.  
 [COFACTOR] Metrahydrobiopterin (BH4). May stabilize the dimeric form of the enzyme.  
 [ENZYME REGULATION] Stimulated by calcium/calmodulin.  
 [SUBUNIT] Homodimer.  
 [SIMILARITY] Belongs to the NOS family.  
 [SIMILARITY] Contains 1 flavodoxin-like domain.  
 FEATURES Location/Qualifiers  
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           /organism="Bos taurus"  
           /db\_xref="taxon:9913"  
     gene 1..1205  
           /gene="NOS3"  
     Protein 1..1205  
           /gene="NOS3"  
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           /EC\_number="[1.14.13.39](#)"  
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Site 26  
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/note="S-palmitoyl cysteine."

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Region 76..79  
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Region 80..83  
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Region 86..89  
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Region 122..139  
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Region 140..141  
/gene="NOS3"  
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Region 143..144  
/gene="NOS3"  
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/note="Phosphoserine (by PKA)."

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Region 165  
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/region\_name="Conflict"  
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Site 186  
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Region 187..188  
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Region 201..202  
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Region 293..296  
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Region 298..299  
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/experiment="experimental evidence, no additional details  
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Region 303..305  
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Region 309..311  
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Region recorded"  
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Region 318..328  
/gene="NOS3"  
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Region 389..390  
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Region 392..394  
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Region 422..440  
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/experiment="experimental evidence, no additional details recorded"

Region 447..450  
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Region 453..455  
/gene="NOS3"  
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Region 455  
/gene="NOS3"  
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/note="S -> Y (in Ref. 3)."

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Region 459  
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Region 460..463

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Region 472..476
/ gene="NOS3"
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/ experiment="experimental evidence, no additional details
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Region 492..512
/ gene="NOS3"
/ region_name="Region of interest in the sequence"
/ inference="non-experimental evidence, no additional
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/ note="Calmodulin-binding (Potential)."
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Site 497

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/ gene="NOS3"
/ site_type="modified"
/ experiment="experimental evidence, no additional details
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/ note="Phosphothreonine (by PKA)."
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Region 514..1162

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/ gene="NOS3"
/ region_name="CysJ"
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[Inorganic ion transport and metabolism]; COG0369"
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Region 522..705

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/ gene="NOS3"
/ region_name="Domain"
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/ note="Flavodoxin-like."
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Region 524..>671

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/ gene="NOS3"
/ region_name="Flavodoxin_1"
/ note="Flavodoxin; pfam00258"
/ db_xref="CDD:40355"
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Site 635

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/ gene="NOS3"
/ site_type="modified"
/ experiment="experimental evidence, no additional details
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/ note="Phosphoserine."
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Site 651..682

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/ gene="NOS3"
/ site_type="np-binding"
/ inference="non-experimental evidence, no additional
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/ note="FMN (By similarity)."
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Region 741

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/ gene="NOS3"
/ region_name="Conflict"
/ experiment="experimental evidence, no additional details
recorded"
/ note="T -> A (in Ref. 3)."
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Region 754..981

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/ gene="NOS3"
/ region_name="FAD_binding_1"
/ note="FAD binding domain; pfam00667"
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/note="L -> V (in Ref. 3)."  
Region 907..908  
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/region\_name="Conflict"  
/experiment="experimental evidence, no additional details recorded"  
/note="WF -> LV (in Ref. 3)."  
Site 937..947  
/gene="NOS3"  
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/inference="non-experimental evidence, no additional details recorded"  
/note="FAD (By similarity)."  
Region 1010..1128  
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/note="Oxidoreductase NAD-binding domain; pfam00175"  
/db\_xref="CDD:40275"  
Site 1012..1030  
/gene="NOS3"  
/site\_type="np-binding"  
/inference="non-experimental evidence, no additional details recorded"  
/note="NADP (By similarity)."  
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/gene="NOS3"  
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/experiment="experimental evidence, no additional details recorded"  
/note="A -> H (in Ref. 3)."  
Site 1110..1125  
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/site\_type="np-binding"  
/inference="non-experimental evidence, no additional details recorded"  
/note="NADP (By similarity)."  
Site 1179  
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/site\_type="modified"  
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## ORIGIN

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181 rnaprcvgri qwgklqvfa rdcssaquemf tyicnhikya tnrgnlrsai tvfpqrapgr
241 gdfriwnsql vryagyrqqd gsvrgdpanv eitelcihg wtpgngrfdv lp1llqapde
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361 steigtrnlc dphryniled vavcmdldtr ttsslwkdka aveinlavlh sfqlakvtiv
421 dhhaatvsfm khldneqkar ggcpadwawi vppisgsltp vfhqemvnyi lspafryqpd
481 pwkgsatkga gitrkktfke vanavkisas lmgtlmakrv katilyaset graqsyaqql
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661 hfcafaravd trleelgger llqlgqgdel cgqeeafrgw akaafqasce tfcvgeeaka
721 aaqdifspkr swkrqyrls tqaeglqlp glihvhrkm fqatvlsven lqsskstrat
781 ilvrltagq eglqyqpgdh igicppnrpg lveallsrve dpppptesva veqlekgspg
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1201 dtpgp
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